

## **REMARKS**

### **I. The Office Action**

The Office rejected all of the pending claims under 35 U.S.C. § 112, first paragraph, for allegedly lacking adequate written description in the specification; and/or under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite. Reconsideration of these rejections is requested.

### **II. Interview Summary**

The Applicants acknowledge with thanks the consideration extended by Examiners Kubelik and Grunberg to the undersigned attorney, to inventor David Fischhoff, to Monsanto attorney T.K. Ball, and to attorney Heather Kissling during an in-person interview on March 3, 2009, when the issues raised in the Office action were discussed. The Applicants agree with the Office's interview summary of issues discussed, and in some cases resolved. (The Applicants continue to disagree with the Office with respect to unresolved issues, for reasons of record.)

### **III. The Amendments to the Specification and Claims**

At the time of the Action, claims 47-70, 73, and 77-141 were pending. In this amendment, claims 48, 52, 58, 81, 84, 87, 91-92, 97, and 99 have been cancelled; new claims 142-163 have been added; and most other claims have been amended. No new matter has been added by way of these amendments.

The dependencies of many claims have been amended, often to increase the number of claims to which a dependent claim refers, because it is believed that the claims are now close to allowance.

Some claims (e.g., claim 47, 51, 61, 62, 119 and 120) have been amended to remove the word "plurality" simply because the word now appears to be redundant in these claims, and not for reasons relating to patentability.

Claims 108 and 131 were amended and new claim 142 was added to divide the subject matter of claim 108 (chloroplast transit peptide or secretory signal peptide) into two separate claims.

Claims 122 and 126 (and new claims 146 and 147) introduce a new step relating to making a DNA construct with the structural gene made according to earlier steps in the method. There is support throughout the specification for making such a DNA construct, which can function as a chimeric gene, including, for example, at page 30, lines 21-24. The elements recited in the step include the structural gene and a promoter. Addition of a promoter already is recited generically in existing claims (see, e.g., claim 107), and finds support throughout the application, including at page 30, lines 12-20. Claim 126 was amended in step (a) to provide context for the starting sequence (ATTTA and polyadenylation signals) that is similar to other claims. New claim 144 is an independent claim with similar steps relating to making a DNA construct with a structural gene made according to a method of the invention and flanking sequences. The addition of a 3' sequence that contains a non-translated polyadenylation signal as specified in claim 144 finds support throughout the specification, including at page 32, lines 6-18; and a similar limitation has been previously presented (see, e.g., claim 109).

New claims 142 and 143 are similar to existing dependent claims and thus raise no new issues. As explained in greater detail below, new claims 145-146 are analogous to claims 112 and 126, and also raise no new issues.

Claims 55, 113, 115, 122, 123, and 148-150 introduce a new limitation pertaining to reducing the number of polyadenylation signals sequences (or the number of ATTTA sequences) “by substituting codons while maintaining the encoded amino acids” (or “maintaining the amino acid sequence”). These limitations finds support in the specification (e.g., at page 24, lines 1-3, and page 25, lines 4-6) and original claim 9. This clause provides a connection between the starting material and the finished structural gene, which renders moot a concern that was raised with respect to some claims under 35 U.S.C. § 112, paragraph 2.

New claims 148-163 are generally directed to the same subject matter as previously presented claims, but are presented in Jepson format.

A few of the amendments correct typographical issues or improve the consistency of the claims.

Most of the remaining amendments are intended to further prosecution by rendering moot the Patent Office's rejections, and are discussed in detail below in relation to specific rejections. These amendments generally serve to conform the claims to subject matter that the Office has acknowledged (e.g., in the Office action or interview summary) satisfy 35 U.S.C. § 112. These amendments are solely to expedite allowance, and not an acquiescence to the merits of any rejection (which are traversed for reasons of record). Amendments relating to one claim are not intended to limit the scope of any claim that does not depend from the amended claim.

#### **IV. The Rejection Under 35 U.S.C. § 112, First Paragraph, Should Be Withdrawn.**

The Office rejected claims 47-70, 73, and 77-141 under 35 U.S.C. § 112, first paragraph, alleging inadequate written description. (Office Action at pages 2-9, section 3.) These rejections are respectfully traversed, and also are rendered moot by amendment, as explained below in greater detail.

##### **A. The starting sequences recited in all of the claims are adequately described in the specification.**

In section 3, part (a), the Office rejected claims 47, 51, 63, 112, 113, 117 and 119, alleging that “[n]either the instant specification nor the originally filed claims appear to provide support for modifying any insecticidal protein coding sequence derived from **any Bacillus species ....**” (Emphasis added.) In related part (g), the Office rejected claim 126, alleging inadequate support for “the concept of the starting material being the coding sequence for **any insecticidal protein ....**” (Emphasis added.) The Office acknowledges that support exists for starting with *Bacillus thuringiensis* insecticidal sequences (as well as for other generic claims). Applicants disagree with the rejections for all of the reasons of record. Solely to expedite allowance, each of the claims rejected in part (a) has been amended to specify “*Bacillus thuringiensis*,” rendering moot this basis for rejection. Claim

126 has been amended to specify “starting with an amino acid sequence of a protein” (a more generic term with acknowledged support), rendering moot the rejection in part (g). Thus, the rejections should be withdrawn.

Claim 128, though not rejected on this basis, also has been amended to include a limitation relating to an insecticidal protein derived from *B.t.*

**B. The rejection relating to coding sequences “devoid or substantially devoid of ATTTA sequences or polyadenylation signal sequences” is moot.**

In section 3, part (b), of the Action, the Office rejected claims on two related bases. The Office rejected claims 47, 51, 55, 59, 113, 119, 120, 122 and 124, alleging inadequate support “for the concept of producing a coding sequence that has a reduction of polyadenylation signal sequences but not ATTTA sequences and vice versa.” (Office Action at pp. 6-7.) The Office also rejected claims 63, 67, 112, 114, 117, 126, 128, alleging inadequate support in the specification “for the concept of producing a coding sequence that is devoid or substantially devoid of polyadenylation signal sequences but not devoid or substantially devoid of ATTTA sequences and vice versa ....” (Office Action at p. 6.)

1. Reducing polyadenylation signal sequences without reducing ATTTA sequences.

With respect to the concept of reducing occurrences of one type of problem sequence but not the other, the Office acknowledged (in the interview summary) that there are original claims (e.g., claims 1 and 2) that evince clear support for removing polyadenylation signal sequences, without the necessity of removing ATTTA, as an aspect of the invention. (See also original claims 30-32.) There also is at least one example in the application that involved removing only polyadenylation signal sequences (Example 1, species containing “BTK240” modifications). The interview summary acknowledges support for “removing some or all of polyA, or some or all of both polyA and ATTTA.” The Office Action also acknowledges that support exists for “one [of polyA and ATTTA] is eliminated and the other reduced.” (Office Action at p. 7.)

Even though the application contemplates removal of **either** the polyadenylation signals OR the ATTTA as an aspect of the invention, Applicants have

amended the claims to conform to subject matter that the Office acknowledges to be adequately described. Specifically, claims 47, 59, 113, 119, 120, 122 and 124 are amended to specify reductions in polyadenylation signal sequences (without also requiring reduction in ATTTA sequences). Dependent claims 49, 60, 115, 121, 123, 125 and 127 further specify reducing ATTTA sequences, analogous to original claims 1, 2 and 30-32. Thus, the rejection of these claims is moot, and should be withdrawn.

In addition, claims 51, 55, and 67 have been amended to specify reduction of ATTTA sequences and polyadenylation signal sequences, another class of subject matter for which the Office acknowledges description in the specification. The interview summary acknowledges support for “removing ... some or all of both polyA and ATTTA.” Thus, the rejection of these claims is moot, and should be withdrawn.

2. Substantially devoid of polyadenylation or ATTTA, without necessarily being substantially devoid of the other.

The Office rejected claims 63, 67, 112, 114, 117, 126 and 128, alleging inadequate support in the specification “for the concept of producing a coding sequence that is devoid or substantially devoid of polyadenylation signal sequences but not devoid or substantially devoid of ATTTA sequences and vice versa ....” (Office Action at p. 6.) However, the Office clarified its position at the interview and in the interview summary, when the Office acknowledged support for “removing some or all of polyA.” Independent claims 63 and 117 have been amended to specify making a structural gene devoid or substantially devoid of the polyadenylation signal sequences. Claim 128 (as previously presented) is similar. Thus, the rejection is moot with respect to these claims.

The Office acknowledged in the Office Action that support exists for claims that specify substantially devoid of both types of problem sequences. (See Office Action at p. 7, citing, e.g., original claims 13 and 33.) Claims 112 and 126 have been amended in this manner, rendering moot the rejection of the claims. New claims 145 and 146 are similar to original claims 112 and 126, respectively, but the new claims specify making a structural gene devoid or substantially devoid of the polyadenylation signal sequences. For the reasons discussed in the preceding paragraph, the rejection should not be applied to these new claims.

The interview summary acknowledges support in the specification for removing “some or all of both polyA and ATTTA.” Claims 67 and 68 have been amended in this manner, rendering the rejection of claim 67 moot.

Claim 114 has been substantially amended such that it depends from claim 113, which is free of the rejection as discussed above in subsection B.1.

The Office also acknowledged in its rejection that the specification provides support for *reducing* one of these types of problem sequences and eliminating (or substantially eliminating) the other, e.g., in the passages at pages 22-23 of the application (“It is most preferred that substantially all the polyadenylation signals and ATTTA sequences are removed although enhanced expression levels are observed with only partial removal of either of the above identified sequences.”). (See Office Action at p. 7: “this means one is eliminated and the other reduced....”) To expedite allowance, a number of claims have been amended in this manner. For example, claim 50 has been amended to specify devoid or substantially devoid of ATTTA sequences **or** devoid or substantially devoid of polyadenylation signal sequences. Claim 50 depends from claim 49, which specifies reducing ATTTA sequences; claim 49 depends from claim 47, which specifies reducing polyadenylation signal sequences. Thus, because claim 50 depends from both claims 49 and 47, claim 50 specifies that **both** ATTTA and polyadenylation signal sequences **are reduced**; and the text of claim 50 further requires that one or the other is eliminated or substantially eliminated (“devoid or substantially devoid”). Claim 53 (dependent from 51); claim 56 (dependent from claim 55); and 61 (dependent from 60/59) are similarly amended. Thus, the claims conform with the Office’s interpretation of the specification, and the rejection should be withdrawn.

**C. The rejection relating to “multiple starting sequences” is moot and should be withdrawn.**

In paragraph 3, part (c) of the Action, the Office rejected claims 55 and 67, alleging lack of adequate description “for the starting material being sequences encoding portions of any two or more insecticidal polypeptides, as in claims 55 and 67. The only multiple starting sequences originally conceived are specific B.t. insecticidal proteins.” (Office Action at p. 8.) The Patent Office rejected claims 91-92 and 113-114 for related reasons.

The Applicants continue to traverse the rejection for reasons of record. The Examples in the application would be understood to be representative, and not limiting, and a person skilled in the art would have concluded from reading the application that fusions of *B.t.* insecticidal proteins were contemplated, in a generic sense. However, the rejected claims have been cancelled (claims 91 and 92) or amended (claims 55, 67 and 114) in manners that render moot the rejection, which should now be withdrawn. (Claim 113 was previously amended to render moot this rejection, and should not have been rejected on this ground.)

#### **D. Conclusion as to Written Description**

For the foregoing reasons, one of ordinary skill in the art would have understood Applicants to be in possession of the invention as presently claimed, so the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

### **V. The Rejections Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn.**

The Patent Office rejected claims 47-112, 117, 118, and 120-141 under 35 U.S.C. § 112, second paragraph, alleging failure to particularly point out and distinctly claim the invention.

#### **A. The term "substantially devoid" is not indefinite as used in the claims.**

In section 4 of the Action, the Office rejected claims 63-68, 112, 117-118 and 126-129, contending that "substantially devoid" is a relative term rendering these claims indefinite. Applicants respectfully traverse.

The law supports Applicants' position that the claims are not indefinite. Recitation of "substantially" to modify a claim term does not render a claim indefinite when the recitation serves to reasonably describe the claimed invention to those of skill in the art. *Andrew Corp. v. Gabriel Elec., Inc.*, 847 F.2d 819, 821-22 (Fed. Cir. 1988) ("The criticized words are ubiquitous in patent claims."). "Substantially devoid" need not have a fixed meaning (i.e., fixed upper limit) to satisfy Section 112, second paragraph.

This rejection was discussed during the interview, and the Office indicated, during the interview and in the Office's interview summary, that this rejection would be

withdrawn. Applicants acknowledge with thanks the Office's willingness to reconsider its position on this issue.

**B. The rejections alleging lack of antecedent basis are moot.**

At page 12 of the Action, the Office alleges that claims 59-62, 70 and 80 were indefinite due to alleged lack of antecedent basis for "the wild-type *Bacillus* gene sequence(s)." The allegedly indefinite term has been deleted or replaced with a reference to wild-type *Bacillus thuringiensis* (*B.t.*) gene sequence(s), which has clearer antecedent basis, rendering moot the rejection.

The Office alleges that claims 95 and 96 were indefinite due to alleged lack of antecedent basis for "the insecticidal protein derived from *Bacillus*." These claims now recite "*Bacillus thuringiensis*" which has clearer antecedent basis in the parent claims, rendering moot the rejection.

**C. The method claims do not omit essential steps.**

At pages 11-12 of the Action, the Office contends that claims 47, 51, 55, 120, 122 and 124 are incomplete for failing to recite an essential step of the claimed method, and has rejected the claims alleging that they are indefinite. The Patent Office said, "The omitted steps are: making the structural gene comprising a coding sequence that encodes the protein of step (a). As currently written there is no connection between the starting material of part (a) and the making step (c) except the substituted codons -- the rest of the codons of the coding sequence of step (a) are not necessarily involved in step (c)." (Office Action at p. 11, section 9(c).)

The Applicants respectfully traverse for all of the reasons of record. No additional step is essential to practice the method. While the application teaches that, in some variations of the invention, the starting material and the modified gene should encode the same protein (e.g., original claim 3), it is clear that the invention does not require this.<sup>1</sup>

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<sup>1</sup> By the time that the application was filed, scientists were able to make mutations to proteins that were not activity-destroying, and the invention would be expected to work in such circumstances. The method focuses on improving expression based on elimination of problem sequences within a coding sequence, and the expression should be improved irrespective of whether the amino sequence is unchanged. (See Rule 132 Declaration of Dr. James Baum, submitted August 20, 2008, at paragraph 10.2.)

Nonetheless, claim amendments have rendered the rejection moot for many claims. For example, the last step in each of claims 47, 120 and 124 has been amended to specify “the” protein.

Claims 51, 55, 67 and 122 require a different analysis. These claims, as amended, specify that modifications be made to a portion of a coding sequence. The claims further specify that making a structural gene with the portion as modified. Thus, there is an explicit connection between the starting material of part (a) and the making step (c) – not merely the substituted codons, but the entire portion in which the modifications have been made. In other words, the rest of the codons of the modified portion are still involved in step (c).

#### **D. Conclusion as to Definiteness**

For the above reasons, the claims particularly point out and distinctly claim the invention, and the rejection under Section 112, second paragraph, should be withdrawn.

#### **VI. Conclusion**

In view of the above amendment, Applicants believe the pending application is in condition for allowance. The Examiner is invited to contact the undersigned attorney by telephone if there are issues or questions that might be efficiently resolved in that manner.

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